

**Remarks**

No amendments were made to the claims.

**1. Claim to Priority**

The subject application is a continuation-in-part of 08/857,288, now patented as U.S. Patent 6,143,738 ("the '738 patent"). The Examiner asserts that the '738 patent fails to provide adequate support under 35 U.S.C. § 112 for claims 14-30 as to methods for reducing blood cholesterol levels in a mammal, "since the parent case merely discloses a method for treating diabetes and/or obesity in a mammal." In light of this assertion by the Examiner and the fact that the subject application contains claims to reducing blood cholesterol levels and blood glucose levels in a mammal, the Examiner has denied the subject application the priority filing date of the '738 patent and restricted the filing date of the subject application to its actual filing date of July 13, 2000. (Note: the Examiner mistakenly recites the filing date as July 14, 2000).

As indicated on its face, the '738 patent is a continuation-in-part of 08/487,443, now patented as U.S. Patent 5,847,172 ("the '172 patent"). The '738 patent refers to the '172 patent in its specification and indicates that the disclosure of the '172 patent is incorporated by reference. See, e.g., column 1, lines 59-62. Accordingly, the subject application, through its priority claim to the '738 patent, and this incorporation by reference statement in the '738 patent, may also rely on the teaching of the '172 patent. The '172 patent has a filing date of June 7, 1995 and describes the use of aminosterols for the treatment and/or prevention of diabetes in a mammal. See, e.g., column 84, line 32 through column 85, line 12. Therefore, the claims in the subject application that are directed to a method for reducing blood glucose levels in a mammal suffering from diabetes comprising the administration of a compound of a structural formula that encompasses various aminosterols, are entitled to the June 7, 1995 filing date of the '172 patent.

**2. Rejection under 35 U.S.C. § 103(a)**

Claims 14-30 are rejected under 35 U.S.C. § 103(a) as being unpatentable over U.S. Patent 5,792,635 to Zasloff *et al* ("the '635 patent") or U.S. Patent 5,842,740 to Zasloff *et al*. in view of the Merck Manual of Diagnosis and Therapy ("the Merck Manual"). The Examiner asserts that the '635 patent and U.S. Patent 5,842,740 describe the use of compound 1436 as an anti-arteriosclerotic and for the treatment of diabetes. The Examiner acknowledges that neither the '635 patent nor U.S Patent 5,842,740

expressly discloses the use of aminosterols for treating serum cholesterol or reducing blood cholesterol levels in a mammal but relies on the Merck Manual for allegedly teaching that elevated serum cholesterol, hypertension diabetes mellitus and obesity are the major risk factors for atherosclerosis. Thus, according to the Examiner, it would have been obvious to a person of ordinary skill in the art to employ the particular aminosterols described in the '635 patent and U.S. Patent 5,842,740 for treating serum cholesterol or reducing blood cholesterol levels in a mammal.

Applicants again bring to the Examiner's attention that U.S. Patent 5,842,740 is not pertinent to any aspect of Applicants' claimed invention, and that the Examiner may have instead intended to cite U.S. Patent 5,840,740 ("the '740 patent") which has at least one of the same inventors, Zasloff, as the subject application. For the purposes of this response, Applicants will assume that it is the '740 patent which has been cited by the Examiner.

Applicants respectfully disagree with the Examiner's assessment and applicability of the '635 or '740 patent disclosures, in view of the Merck Manual, to the claimed invention for at least the reasons discussed below.

*Reducing Blood Glucose Levels*

As discussed above in section 1, Applicants believe that the claims of the subject application directed to a method of reducing blood glucose levels are entitled to the June 7, 1995 filing date of the '172 patent. The '635 patent also has a filing date of June 7, 1995, which means that the '635 patent doesn't qualify as prior art to Applicants' claims directed to a method of reducing blood glucose levels. Similarly, the '740 patent also has a filing date of June 7, 1995. Applicants note that the specification of the '740 patent states that "the application is related to U.S. Ser. No. 08/416,883, which is the U.S. national phase of International application Ser. No. PCT/US94/10265, filed Sep. 13, 1994." A review of the specification of the 08/416,883 application (now U.S. Patent 5,733,899) reveals no disclosure of diabetes, blood glucose or cholesterol. Therefore, as it pertains to the pending claims in the subject application, the '740 patent is limited to its actual June 7, 1995 filing date. As such, the '740 patent also doesn't qualify as prior art to the subject application regarding Applicants' method claims directed to reducing blood glucose levels. The Merck Manual cannot remedy the defects present in the '635 and the '740 patents. Applicants therefore respectfully request that the rejection of claims 17-25, 29 and 30, directed to a method of reducing blood glucose levels, be withdrawn at least for the above-stated reasons.

Reducing Blood Cholesterol Levels

Claims 14-16 and 20-28 are directed to a method of reducing blood cholesterol levels. The Merck Manual defines arteriosclerosis as a “generic term for several diseases in which the arterial wall becomes thickened and loses elasticity” (page 1654). The Examiner cites the Merck Manual for indicating elevated levels of low density lipoprotein (LDL) and reduced levels of high density lipoprotein as risk factors for atherosclerosis.

Applicants respectfully disagree with the Examiner’s assertions. Atherosclerosis is defined by the Merck Manual as “a form of arteriosclerosis characterized by patchy subintimal thickening (atheromas) of medium and large arteries, which can reduce or obstruct blood flow” (page 1655). Therefore, according to the Merck Manual cited by the Examiner, “arteriosclerosis” is not the same as “atherosclerosis” because arteriosclerosis is a term encompassing several diseases (and likely several different causes for disease), while atherosclerosis is a particular form of arteriosclerosis. The ‘635 and ‘740 patents refer only to anti-arteriosclerotic agents and do not teach or suggest the narrower anti-atherosclerotic agents. Thus, a person of ordinary skill in the art would not be motivated with an expectation of success to prepare aminosterols for reducing blood cholesterol levels based on a sentence in the ‘635 or ‘740 patents stating that various NHE-specific inhibitors may provide anti-arteriosclerotic agents. This is especially true since undoubtedly at least some manifestations of arteriosclerosis are not due to elevated levels of blood cholesterol.

Further, treatment of a risk factor is not the same as treating a disease state that may have resulted, in part, from the risk factor. Elevated blood cholesterol levels are associated with many diseases and/or pathological states, including stroke, myocardial infarction, Cushing’s syndrome, Alstrom syndrome, diabetes, Amaurosis fugax, hypervitaminosis, *etc.* Thus, it would not be obvious to assume that just because a compound may be effective in treating a disease state, that it would necessarily also be effective in preventing or treating a particular symptom (*e.g.*, elevated blood cholesterol levels) that may eventually lead to the expression of that disease state. For at least these reasons, Applicants request that this rejection be withdrawn.

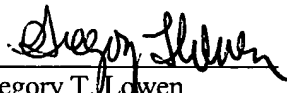
**3. Conclusion**

Upon consideration of the foregoing, it will be recognized that Applicants have fully and appropriately responded to all of the Examiner’s rejections. Accordingly, the claims are believed to be in proper form in all respects and a favorable action on the merits is respectfully requested.

Except for issue fees payable under 37 C.F.R. § 1.18, the Commissioner is hereby authorized by this paper to charge any additional fees during the entire pendency of this application, including fees due under 37 C.F.R. §§1.16 and 1.17 which may be required, including any required extension of time fees, or to credit any overpayment to Deposit Account No. 50-0310. This paragraph is intended to be a **CONSTRUCTIVE PETITION FOR EXTENSION OF TIME** in accordance with 37 C.F.R. § 1.136(a)(3).

Respectfully Submitted,

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Gregory T. Lowen  
Registration No. 46,882  
Direct: 202-739-5915

**CUSTOMER NO. 009629**  
MORGAN, LEWIS & BOCKIUS LLP  
1111 Pennsylvania Avenue, N.W.  
Washington, D.C. 20004  
Tel: 202-739-3000  
Fax: 202-739-3001